

Patent claims

1. Device for cultivating cells in liquid columns on a millilitre scale, having a container for receiving a liquid culture suspension of the cells,
an agitation system for mixing the culture suspension in the container about a mixing axis,
characterised in that
the container and/or the agitation system are configured in such a manner that the flow velocity is modified locally and/or temporally along a streamline or flow line about the agitation axis.
2. Device according to the preceding claim, characterised in that the container and/or the agitation system are configured in such a manner that, by means of the agitation system, conveyance of the culture suspension which is directed from the suspension surface to the base of the container is effected.
3. Device according to the preceding claim, characterised in that the conveyance of the culture suspension has a component which is axial with respect to the mixing axis.
4. Device according to one of the preceding claims, characterised in that the inner walls of the container which enclose the culture suspension have, below, in and/or above the rotational plane of the agitation system, a non-rotationally symmetrical form.
5. Device according to one of the preceding claims, characterised in that the inner walls of the container which enclose the culture suspension form, below, in and/or above the rotational plane of the

agitation system, a polygon, preferably with four, five, six or more corners.

6. Device according to one of the preceding claims, characterised in that the rotational axis of the agitation system is disposed off-centre or eccentically in the container with respect to the inner walls of the container which enclose the culture suspension.
7. Device according to one of the preceding claims, characterised in that at least one baffle is disposed on the inner wall of the container along the circumference of the agitation system.
8. Device according to one of the preceding claims, characterised in that one, two, three, four or more baffles are disposed along the inner wall of the container, at a spacing, advantageously at a uniform spacing, relative to each other.
9. Device according to one of the two preceding claims, characterised in that the baffle or baffles is or are disposed below, in and/or above the rotational plane of the agitation system.
10. Device according to one of the three preceding claims, characterised in that the agitation system and the baffle are disposed at a minimum gap spacing relative to each other of 0.05 mm to 20 mm, preferably 0.1 mm to 3 mm.
11. Device according to one of the preceding claims, characterised in that the container is a flask, a reagent glass or a cavity of a microtitre plate or of another plate which is provided with cavities.
12. Device according to one of the preceding claims, characterised in that the agitation system is magnetically positioned and/or driveable.

13. Device according to one of the preceding claims, characterised in that the agitation system is mounted or not mounted.
14. Device according to one of the preceding claims, characterised in that the agitation system is mounted via a shaft and if necessary is driveable via the shaft.
15. Device according to the preceding claim, characterised in that the shaft and the baffle or baffles are configured in one piece.
16. Device according to one of the claims 6 to 9, 13 and 14, characterised in that the shaft and the baffle or baffles is or are insertable into the container.
17. Device according to one of the claims 13 to 16, characterised in that the shaft protrudes into the container from above.
18. Device according to one of the preceding claims, characterised in that the shaft is enlarged at its lower end or has a flange.
19. Device according to one of the claims 13 to 18, characterised in that the shaft is configured as a solid material shaft or as a hollow pipe.
20. Device according to one of the preceding claims, characterised in that the shaft is configured as a hollow pipe and a nozzle is disposed on its end which is open at the bottom.
21. Agitation system having a basic body which, in operation, has an upper side and an underside,
characterised in that,
in the basic body, at least one first through-channel is disposed, the first opening of which is situated at least partially on the underside

of the basic body and the second opening of which is situated on the upper side and/or laterally on the basic body.

22. Agitation system according to the preceding claim, characterised in that, in the basic body, at least one first boring is disposed as first through-channel, the passage axis of which boring includes an angle α with $0^\circ \leq \alpha < 90^\circ$ with the rotational axis of the agitation system, said angle opening to the upper side of the agitation system.
23. Agitation system according to one of the two preceding claims, characterised in that, in the basic body, at least one further second through-channel is disposed, the first opening of which is situated at least partially on the upper side of the basic body and the second opening of which is situated on the underside and/or laterally on the basic body.
24. Agitation system according to the preceding claim, characterised in that, in the basic body, at least one second boring is disposed as second through-channel, the passage axis of which boring includes an angle α with $0^\circ \leq \alpha < 90^\circ$ with the rotational axis of the agitation system, said angle opening to the underside of the agitation system.
25. Agitation system according to one of the two preceding claims, characterised in that the first and the second through-channel intersect and/or the first and the second through-channel meet each other and, forming a common through-channel, emerge laterally from the agitation system.
26. Agitation system according to one of the claims 21 to 25, characterised in that two or more first and/or second through-channels are disposed along the circumference of the agitation system at a uniform spacing relative to each other.

27. Agitation system according to one of the claims 21 to 26, characterised in that the basic body, in the cross-section perpendicular to the rotational axis, is circular cylindrical, elliptical, polygonal, square or rectangular.
28. Agitation system according to one of the claims 21 to 27, characterised in that the basic body is oval, egg-shaped or cuboid.
29. Agitation system according to one of the claims 21 to 28, characterised in that the basic body has recesses along its circumferential edge in the rotational direction.
30. Agitation system according to one of the claims 1 to 20, characterised in that the agitation system is configured according to one of the claims 21 to 29.
31. Arrangement for parallel, automated cultivation of cells in liquid columns on a millilitre scale, characterised by
at least one device or agitation system according to one of the preceding claims.
32. Arrangement according to the preceding claim, characterised by a block, in which a number of cavities, which corresponds to the number of containers, are disposed, which represent containers themselves or are configured for receiving containers.
33. Arrangement according to the preceding claim, characterised in that the cavities are configured as borings with a diameter corresponding to the external diameter of the containers.

34. Arrangement according to one of the two preceding claims, characterised in that means for moderating the temperature of the block, means for driving the magnetic agitation system and/or a sterile gas supply to the containers are disposed in the block.
35. Arrangement according to one of the claims 30 to 34, characterised in that the containers, the arrangement and/or the block are sealed in a sterile manner on their or its upper side by means of a cover.
36. Arrangement according to the preceding claim, characterised in that the cover has an opening for the release of gases and as access to the interior of the container or block, which opening extends in a straight line and longitudinally from the interior to the outer side of the cover and connects these together in an open manner for gas convection.
37. Arrangement according to the preceding claim, characterised in that, in the interior, a higher gas pressure is present than on the outer side of the cover.
38. Arrangement according to one the two preceding claims, characterised in that the opening has the form of a boring or of a tube.
39. Arrangement according to one of the three preceding claims, characterised in that the opening has a clearance width, which makes possible the introduction of a sampling element or of a sensor, a pipette tip, a piercing cannula, a pH electrode or another object or elongated object into the interior of the container or block.
40. Arrangement according to one of the claims 36 to 39, characterised in that the opening is a tube made of metal or metal alloys, advantageously made of aluminium and/or silver.

41. Arrangement according to one of the claims 36 to 40, characterised by container separating elements which, when in the state set upon the containers or the block, separate individual containers from each other in a gas- and/or liquid-impermeable manner.
42. Arrangement according to one of the claims 36 to 41, characterised in that the cover has a sterile gas supply to the one or a plurality of containers, for all the containers together or for a plurality or each of the containers separately.
43. Arrangement according to the preceding claim, characterised in that the sterile gas supply has gas distributor structures which are integrated in the cover or disposed adjacent to the cover.
44. Arrangement according to the preceding claim, characterised in that channels are disposed in the cover as gas distributor structures.
45. Arrangement according to the preceding claim, characterised in that the channels between the gas inlet into the gas distributor structure and the gas outlets into the respective containers all have the same length and/or the same number of bends.
46. Arrangement according to one of the claims 41 to 45, characterised in that the gas supply is connected to a gas feed, if necessary via sterile filters and/or air humidifiers.
47. Arrangement according to one of the claims 31 to 46, characterised in that the cover has at least one planar layer or flat plate, which covers the opening of the at least one container.
48. Arrangement according to the preceding claim, characterised in that it has at least two planar layers which are disposed parallel to each

other and between which the gas distributor structures are disposed.

49. Method for cultivating cells in liquid columns on a millilitre scale, at least one cell suspension being moved in a container in such a manner that the cell suspension forms an annular flow,
characterised in that
the flow velocity of the annular flow is modified locally and/or temporally along a streamline.
50. Method according to the preceding claim, characterised in that the container and/or the agitation system are configured in such a manner that conveyance of the culture suspension which is directed from the suspension surface to the base of the container is effected.
51. Method according to one of the two preceding claims, characterised in that the at least one cell suspension is cultivated in a device or arrangement according to one of the preceding claims by mixing with a agitation system.
52. Method according to the preceding claim, characterised in that the agitation system is driven with 1 to 4000 revolutions per minute.
53. Method according to one of the two preceding claims, characterised in that the agitation system is driven with over 500 revolutions per minute.
54. Method according to the preceding claim, characterised in that the agitation system is driven with over 1000 revolutions per minute.